

CLAIMS

1. An antibody with specific affinity for a characteristic epitope of the ED-B domain of fibronectin, wherein the antibody has improved affinity to said ED-B epitope.

2. The antibody according to claim 1, wherein the affinity is in the subnanomolar range.

3. The antibody according to claim 1, wherein the antibody recognizes ED-B(+) fibronectin.

4. The antibody according to claim 1, wherein said antibody is in the scFv format.

5. The antibody according to claim 4, the antibody being a recombinant antibody.

6. The antibody according to claim 4 wherein the affinity is improved by introduction of a limited number of mutations in its CDR residues.

7. The antibody according to claim 6, wherein the residues are residues 31-33, 50, 52 and 54 of VH and two residues 32 and 50 of its VL domain which have been mutated.

8. The antibody according to claim 1, wherein the antibody binds the ED-B domain of fibronectin with a Kd of 27 to 54 pM, most preferably with a Kd of 54 pM.

9. The antibody according to claim 1, being the antibody L19.

10. The antibody according to claim 1 with the following amino acid sequence:

VH (SEQ ID NO: 19)

EVQLLES GGG LVQPGGSLRL SCAASGFTFS
SFSMSWVRQA PGKGLEWVSS ISGSSGTTYY
ADSVKGRFTI SRDNSKNTLY LQMNSLRAED
TAVYYCAKPF PYFDYWGQGT LVTVSS

linker (SEQ ID NO: 20)

GDGSSGGSGGASTG

VL (SEQ ID NO: 21)

EIVLTQSPGT LSLSPGERAT LSCRASQSVS
SSYLAWYQQK PGQAPRLLIY YASSRATGIP
DRFSGSGSGT DFTLTISRLE PEDFAVYYCQ
QTGRIPPTFG QGTKVEIK

11. The antibody according to claim 1, wherein the antibody is a functionally equivalent variant form of L19.

12. The antibody according to claim 9, wherein the antibody is radiolabeled.

13. The antibody according to claim 12, wherein the antibody is radioiodinated.

5 14. Method for rapid angiogenesis targeting wherein an antibody with specific affinity for a characteristic epitope of the ED-B domain of fibronectin, the antibody having improved affinity to said ED-B domain, is used.

15. Method according to claim 14 for immunoscintigraphic detection of angiogenesis.

10 16. Method according to claim 15 for detecting diseases characterized by vascular proliferation such as diabetic retinopathy, age-related macular degeneration or tumours.

17. Method according to claim 14, wherein the antibody localizes the respective tissue three to four hours, most preferably 3 hours after its injection.

15 18. A diagnostic kit comprising an antibody with specific affinity for a characteristic epitope of the ED-B domain of fibronectin, said antibody having improved affinity to said ED-B domain and one or more reagents necessary for detecting angiogenesis.

20 19. Method for diagnosis and therapy of tumours and diseases characterized by vascular proliferation wherein an antibody with specific affinity for a characteristic epitope of the ED-B domain of fibronectin, said antibody having improved affinity to said ED-B domain, is used.

25 20. Conjugates comprising an antibody according to Claim 1 and a molecule capable of inducing blood coagulation and blood vessel occlusion.

21. Conjugates according to claim 20 wherein the molecule capable of inducing blood coagulation and blood vessel occlusion is a photoactive molecule.

22. Conjugates according to claim 21 wherein the photoactive molecule is a photosensitizer.

30 23. Conjugates according to claim 22 wherein the photosensitizer absorbs at wavelength above 600 nm.

24. Conjugates according to claim 22 wherein the photosensitizer is a derivative of

tin (IV) chlorine e6.

25. Method for the treatment of angiogenesis-related pathologies wherein a conjugate according to claim 20 is injected.

26. Method for the treatment of angiogenesis-related pathologies wherein a
5 conjugate according to claim 22 is injected, followed by irradiation.

27. Method according to claim 26 wherein the angiogenesis-related pathology treated is caused by or associated with ocular angiogenesis.

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